"...In re Cofer, 354 F.2d 664, 148 USPQ 268 (CCPA 1966) (Claims to the free-flowing crystalline form of a compound were held unobvious over references disclosing the viscous liquid form of the same compound because the prior art of record did not suggest the claimed compound in the crystalline form or how to obtain such crystals).

It is both routine and customary for USPTO to issue patents that relate to crystalline forms of compounds. *See*, for example, U.S. Pat. Nos. 6,492,379, 6,441,002 and 6,440,459.

1. Claims 1-116 Stand Rejected Under 35 U.S.C. § 102

The Examiner rejected claims 1-116 under 35 U.S.C. § 102 as inherent in the cited reference, Acta. Cryst., (1989, C45, 129-132) by Janes *et al.*, which refers to i) a lamotrigine methanol solvate (monoclinic $P2_1/n$), but lacks a description of how the disclosed form was made; and ii) a second form of lamotrigine crystallized from absolute ethanol (monoclinic space). The only possible solvates would be methonolate and ethanolate.

Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Oelrich and Divigard*, 666 F.2d 578 (CCPA 1981). Anticipation by inherency requires that 1) the missing descriptive matter be "necessarily present" in the prior art reference and that 2) it would be so recognized by persons of ordinary skill in the art. *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). When prior art fails to disclose a method for making a claimed compound, at the time the invention was made, it cannot be legally concluded that the compound itself is in the possession of the public. *Ashland Oil, Inc. v Delta Resins & Refractories, Inc.* 776 F.2d 281 (Fed. Cir. 1985).

With respect to the claimed lamotrigine forms (i.e., B, C, D, F, K, L, M, N, P, R, S and U) other than methanolate and ethanolate forms, there can be no inherency because the preparation of these forms involves organic solvents not disclosed by Janes *et al.*, which will not produce a methanolate or ethanolate.

Applicants have canceled the methanolate and ethanolate forms (i.e., forms E, E1, H, and O) as well as isopropanolate form (i.e., forms J and Q) from the claims without prejudice. Claims 17-21 (directed to methanolate-form E), claims 22-26 (directed to ethanolate-form E1), claims 32-36 (directed to ethanolate-form H), claims 37-41 (directed to isopropanolate-form J), claims 62-66 (directed to methanolate-form O) and claims 72-76 (directed to isopropanolate-form Q) are canceled without prejudice. Applicants reserve the right to prosecute these claims.

Accordingly, Applicants respectfully request reconsideration of withdrawal the 35 U.S.C.§ 102 inherency rejection.

2. **Claim 1 Stand Rejected Under 35 U.S.C. § 112, 2nd Paragraph**

The Examiner alleges that claim 1 fails to particularly point out and distinctly define the metes and bounds of the subject matter sought to be patented. The Examiner bases this rejection on the ground that it fails to provide the chemical structure of the claimed solvate.

35 U.S.C. § 112, 2nd Paragraph requires:

> "The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."

MPEP § 2171 states:

> There are two separate requirements set forth in this paragraph:
> (A) the claims must set forth the subject matter that applicants regard as their invention; and
> (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

MPEP § 2173.05(t) further discusses situations when chemical formula is involved:

> Claims to chemical compounds and compositions containing chemical compounds often use formulas that depict the chemical structure of the compound. These structures should not be considered as indefinite nor speculative in the absence of evidence that the assigned formula is in error...
> ... A rejection under 35 U.S.C. § 112, second paragraph for failure to identify the entire structure was reversed and the court held: "While the absence of such a limitation obviously broadens the claim and raises questions of sufficiency of disclosure, it does not render the claim indefinite." Chemical compounds may be claimed by a name that adequately describes the material to one skilled in the art. *See Martin v. Johnson*, 454 F.2d 746, 172 USPQ 391 (CCPA 1972).

Applicants submit that the present specification and claims describe the lamotrigine compound by its chemical name, which adequately describes the material to one skilled in the art. Applicants also set forth subject matter that applicants regard as their invention. Applicants further define the metes and bounds of the invention by providing the following information: i) identity of solvates for respective crystalline lamotrigine forms; ii) solvate characteristics; for example, monosolvate, sesquisolvate, 2/3 solvate or ½ solvate; and iii) XRD data. Contrary to the Examiner's rejection, there is no requirement that a chemical structure must be present in the claim itself in order to satisfy the 35 U.S.C. § 112, 2nd

paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C.§ 112, 2nd paragraph rejection.

Applicants further address specific rejections raised by the Examiner as follows:

4. **IUPAC Name for Lamotrigine**

Applicants respectfully submit that CAS Registry No. 84057-84-1 is assigned for lamotrigine. The present specification also provides the chemical names for the lamotrigine; namely, 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine or 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine (*See*, specification, page 1, lines 14-15).

Submitted herewith is the CAS Registry No., together with its chemical names and chemical formula (*See*, specification, page 1, lines 17-29), Applicants believe that there should be sufficient information for the Examiner to conduct necessary search for close compounds.

5. **Claims 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, et seq., Stand Rejected under 35 U.S.C. § 112, 2nd Paragraph**

The Examiner alleges that claims 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, et seq., are rejected because they contain reference to a drawing figure. The Examiner alleges that claims must be complete within themselves.

> MPEP § 2173.05(s) states:
> Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citation omitted).

Applicants submit that XRD data used to define a novel crystal form is routinely recognized by the PTO as an exceptional circumstance because there is no comparable way to describe such crystal forms. For example, see: U.S. Pat. Nos. 6,440,459, 6,436,987, and 6,225,474. Accordingly, Applicants respectfully request reconsideration of withdrawal the 35 U.S.C.§ 112, 2nd paragraph rejection. Claims 20, 25, 35, 40, 65, and 75 have been canceled and the rejection against these canceled claims is moot.

6. **Other Rejections**

a) Structure of Compound Claimed in Claim 2

Applicants provide the chemical name for lamotrigine and other information relating i) identity of solvates; ii) solvate characteristics; and, iii) XRD data for crystalline lamotrigine forms. There is no requirement that a chemical structure of a compound as presented in claim 2 included in a claim (see argument above).

b) How Was Compound Obtained?

Applicants respectfully direct the Examiner's attention to, for example, the process described in claim 94. Claim 94 recites:

> A method for preparing a lamotrigine form B, comprising the steps of::
> 1) dissolving lamotrigine anhydrous in dimethylformamide at about 70^0C;
> 2) precipitating the lamotrigine from B by adding water at about 0^0C; and
> 3) filtering the lamotrigine form B.

The supporting example for claim 94 can be found in Example 5 of the specification (page 24, 14-19).

c) Structure of Compounds Claimed in Claims 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52, 57, et seq., Claims 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52, 57, et seq., are rejected under 35 U.S.C. § 112, 2nd Paragraph

The Examiner rejected claims 2, 7, 12, 17, 22, 27, 32, 37, 42, 47, 52, 57, et seq., under 35 U.S.C. § 112, 2nd paragraph. As detailed above, Applicants submit that the present specification and claims describe the lamotrigine compound by its chemical name, which adequately describe the material to one skilled in the art.

Claims 17, 22, 323, 37, 62 and 72 have been canceled and the rejection against these canceled claims is moot.

d) Structure of Solvate Claims in Claims 6, 11, 16, 21, 26, 31, 36, 41, et seq., What is Bonded to What? Claims 6, 11, 16, 21, 26, 31, 36, 41, et seq., are rejected under 35 U.S.C. § 112 as unclear.

The Examiner rejected claims 6, 11, 16, 21, 26, 31, 36, 41, et seq., under 35 U.S.C. § 112, 2nd paragraph. As detailed above, Applicants submit that the present specification and claims describe the lamotrigine compound by its chemical name, together with their respective solvates, which adequately describe the material to one skilled in the art. Accordingly, Applicants respectfully request reconsideration of withdrawal the 35 U.S.C. §112, 2nd paragraph. Claims 21, 26, 36, 41, 6 and 76 have been canceled and the rejection against these canceled claims is moot.

e) Claim 92 Is Improper Composition Claim And Rejected Under 35 U.S.C. § 112 2nd Paragraph, As Forms B, C, D, E, E1, F, H, J, K, L, M, N, O, P, Q, S and U Are Unknown

Claim 92 is now amended to recite a pharmaceutical acceptable carrier.

With respect to the 35 U.S.C. §112, 2nd Paragraph rejection, Applicants reiterate the reasons as above. The rejection should be overcome.

f) Claims 92 and 93 Stand Rejected Under 35 U.S.C. § 103. Forms of Astriazine In Prior Art

MPEP § 2116.01 states:
All the limitations of a claim must be considered when weighing the differences between the claimed invention and the prior art in determining the obviousness of a process or method claim. See MPEP § 2143.03.

In re Ochiai, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and *In re Brouwer*, 77 F.3d 422, 37 USPQ2d 1662 (Fed. Cir. 1996) addressed the issue of whether an otherwise conventional process could be patented if it were limited to making or using a novel, non-obvious product. In both cases, the Federal Circuit held that the use of *per se* rules is improper but required a highly fact-dependent analysis involving taking the claimed subject matter as a whole and comparing it to the prior art.

Here, the cited reference fails to provide any motivation or suggestion to: i) prepare a pharmaceutical composition comprising the claimed crystalline lamotrigine forms and ii) use such a pharmaceutical composition for treating a patient suffering from epilepsia. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C.§ 103 rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully submits that pending claims 1-16, 26-31, 42-61 and 77-123 are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is urged to telephone the undersigned at the number below. The undersigned may also be contacted by email at slo@kenyon.com.

Respectfully Submitted,
KENYON & KENYON

Dated: April 17, 2003 By: _____
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In The Claims:

Claims 1, 92 and 93 have been amended herein as follows:

1. (Amended) A solvated form of crystalline lamotrigine containing a solvate, wherein the solvate is selected from the group consisting of dimethylformamide, dimethylamine, [methanol, ethanol, isopropyl alcohol,] tetrahydrofuran, methyl-isobutyl-ketone, methyl-tertiary-butyl-ether, water and acetone.

92. (Amended) A pharmaceutical composition comprising a therapeutically effective amount of at least one [a] lamotrigine [solvated crystal] form[s, wherein the lamotrigine solvated crystal form is] selected from the group consisting of lamotrigine forms B, C, D, [E, E1,] F, [H, J,] K, L, M, N, [O,] P, [Q,] R, S and U; and, a pharmaceutically acceptable excipient.

93. (Amended) A method for treating a patient suffering from epilepsia by administering a therapeutically effective amount[s] of at least one [a] lamotrigine [solvated crystal] form[s, wherein the lamotrigine solvated crystal form is] selected from the group consisting of lamotrigine forms B, C, D, [E, E1,] F, [H, J,] K, L, M, N, [O,] P, [Q,] R, S, and U.